

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in this application.

1. (Canceled)
2. (Canceled)
3. (Canceled)
4. (Canceled)
5. (Canceled)
6. (Withdrawn) A method for detecting phosphorylated IRS-1 and/or phosphorylated IRS-2 in a biological sample, said method comprising the steps of:
 - (a) contacting a biological sample potentially, or suspected of, containing phosphorylated IRS-1 and/or phosphorylated IRS-2 with at least one antibody of claim 1, under conditions suitable for formation of an antibody-IRS complex; and
 - (b) detecting the presence of said complex in said sample, wherein the presence of said complex indicates the presence of phosphorylated IRS-1 (Ser1101) and/or phosphorylated IRS-2 (Ser1149) in said sample.
7. (Withdrawn) The method of claim 6, wherein said biological sample is obtained from a subject at risk of, or suspected of, having type 2 diabetes.
8. (Withdrawn) The method of claim 6, wherein said biological sample has been contacted with at least one Protein Kinase C (PKC) inhibitor or PKC theta inhibitor, or is obtained from a subject treated with such inhibitor.
9. (Withdrawn) The method of claim 6, wherein said biological sample has been contacted with a compound being tested for inhibition of PKC activity or expression.

10. (Canceled)
11. (Withdrawn) A method for detecting PKC theta activity in a biological sample, said method comprising the steps of:
 - (a) contacting said biological sample with at least one antibody of claim 1 under conditions suitable for formation of an antibody-IRS complex;
 - (b) detecting the presence of said complex in said biological sample, wherein the presence of said complex indicates the presence of phosphorylated IRS-1 (Ser1101) and/or phosphorylated IRS-2 (Ser1149) in said test tissue.
12. (Withdrawn) The method of claim 11, further comprising the step (c) comparing the level of complex detected in step (b) with the level of complex in a control sample with known PKC theta activity, wherein a difference in IRS-1 (Ser1101) and/or IRS-2 (Ser1149) phosphorylation levels between said biological sample and said control sample indicates altered PKC theta activity in said biological sample.
13. (Withdrawn) The method of claim 11, wherein said biological sample is obtained from a subject at risk of, or suspected of, having type 2 diabetes.
14. (Withdrawn) The method of claim 11, wherein said biological sample has been contacted with at least one PKC inhibitor or PKC theta inhibitor, or is obtained from a subject treated with such inhibitor.
15. (Withdrawn) The method of claim 11, wherein said biological sample has been contacted with a compound being tested for inhibition or PKC activity or expression.

16. (Canceled)

17. (Currently Amended) An isolated Insulin Receptor Substrate-1/2 phospho-specific antibody that binds to human Insulin Receptor Substrate-1 (IRS-1) when phosphorylated at serine 1101 (SEQ ID NO: 1), but does not bind human IRS-1 when not phosphorylated at serine 1101.

18. (Previously Presented) The antibody of claim 17, wherein said antibody further binds to human Insulin Receptor Substrate-2 (IRS-2) when phosphorylated at serine 1149 (SEQ ID NO: 2), but does not bind human IRS-2 when not phosphorylated at serine 1149.

19. (Previously Presented) The antibody of claim 17, wherein said antibody further binds to murine IRS-1 when phosphorylated at serine 1095 (SEQ ID NO: 3), but does not bind murine IRS-1 when not phosphorylated at serine 1095.

20. (Previously Presented) The antibody of claim 17, wherein said antibody further binds to murine IRS-2 when phosphorylated at serine 1138 (SEQ ID NO: 4), but does not bind murine IRS-2 when not phosphorylated at serine 1138.

21. (Currently Amended) An isolated Insulin Receptor Substrate-1/2 phospho-specific antibody that binds to human IRS-2 when phosphorylated at serine 1149 (SEQ ID NO: 2), but does not bind human IRS-2 when not phosphorylated at serine 1149.

22. (Previously Presented) The antibody of claim 21, wherein said antibody further binds to human IRS-1 when phosphorylated at serine 1101 (SEQ ID NO: 1), but does not bind human IRS-1 when not phosphorylated at serine 1101.

23. (Previously Presented) The antibody of claim 21, wherein said antibody further binds to murine IRS-1 when phosphorylated at serine 1095 (SEQ ID NO: 3), but does not bind murine IRS-1 when not phosphorylated at serine 1095.

24. (Previously Presented) The antibody of claim 21 wherein, said antibody further binds to murine IRS-2 when phosphorylated at serine 1138 (SEQ ID NO: 4), but does not bind murine IRS-2 when not phosphorylated at serine 1138.25.

25. (Currently Amended) An isolated Insulin Receptor Substrate-1/2 phospho-specific antibody that binds to murine IRS-1 when phosphorylated at serine 1095 (SEQ ID NO: 3), but does not bind murine IRS-1 when not phosphorylated at serine 1095.
26. (Previously Presented) The antibody of claim 25, wherein said antibody further binds to human IRS-1 when phosphorylated at serine 1101 (SEQ ID NO: 1), but does not bind human IRS-1 when not phosphorylated at serine 1101.
27. (Previously Presented) The antibody of claim 25, wherein said antibody further binds to human IRS-2 when phosphorylated at serine 1149 (SEQ ID NO: 2), but does not bind human IRS-2 when not phosphorylated at serine 1149.
28. (Previously Presented) The antibody of claim 25, wherein said antibody further binds to murine IRS-2 when phosphorylated at serine 1138 (SEQ ID NO: 4), but does not bind murine IRS-2 when not phosphorylated at serine 1138.
29. (Currently Amended) An isolated Insulin Receptor Substrate-1/2 specific antibody that binds to murine IRS-2 when phosphorylated at serine 1138 (SEQ ID NO: 4), but does not bind murine IRS-2 when not phosphorylated at serine 1138.
30. (Previously Presented) The antibody of claim 29, wherein said antibody further binds to human IRS-1 when phosphorylated at serine 1101 (SEQ ID NO: 1), but does not bind human IRS-1 when not phosphorylated at serine 1101.
31. (Previously Presented) The antibody of claim 29, wherein said antibody further binds to human IRS-2 when phosphorylated at serine 1149 (SEQ ID NO: 2), but does not bind human IRS-2 when not phosphorylated at serine 1149.
32. (Previously Presented) The antibody of claim 29, wherein said antibody further binds to murine IRS-1 when phosphorylated at serine 1095 (SEQ ID NO: 3), but does not bind murine IRS-1 when not phosphorylated at serine 1095.
33. (Previously Presented) The antibody as in one of claims 17, 21, 25 or 29, wherein said antibody is polyclonal.
34. (Previously Presented) The antibody as in one of claims 17, 21, 25 or 29, wherein said antibody is monoclonal.

35. (Previously Presented) A hybridoma cell line producing any one of the antibodies of claim 34.
36. (Previously Presented) A kit for the detection of phosphorylated human IRS-1 (Ser1101) (SEQ ID NO: 1) in a biological sample, said kit comprising (a) the antibody of claim 17 and (b) at least one secondary antibody conjugated to a detectable group.
37. (Previously Presented) A kit for the detection of phosphorylated human IRS-2 (Ser1149) (SEQ ID NO: 2) in a biological sample, said kit comprising (a) the antibody of claim 21 and (b) at least one secondary antibody conjugated to a detectable group.
38. (Currently Amended) A kit for the detection of PKC theta activity in a biological sample, said kit comprising (a) at least one antibody of claims 17, 21, 25, or 29 that binds phospho IRS-1 or phospho IRS-2 and (b) at least one secondary antibody conjugated to a detectable group.